

17 MAY 2005

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 June 2004 (03.06.2004)

PCT

(10) International Publication Number
WO 2004/045550 A3

(51) International Patent Classification⁷: **A61K 39/00**,
39/02

(21) International Application Number:
PCT/US2003/037013

(22) International Filing Date:
18 November 2003 (18.11.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/427,318 18 November 2002 (18.11.2002) US

(71) Applicant (for all designated States except US): **BOSTON MEDICAL CENTER CORPORATION** [US/US]; One Boston Medical Center Place, Boston, MA 02118 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GENCO, Caroline, A.** [US/US]; 41 Garrison Road, Boston, MA 02445 (US). **GIBSON, Frank, C.** [US/US]; 24 Oakview Terrace, Jamaica Plain, MA 02130 (US).

(74) Agents: **HEINE, Holliday, C. et al.**; Weingarten, Schurgin, Gagnebin & Lebovici, LLP, Ten Post Office Square, Boston, MA 02109 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- of inventorship (Rule 4.17(iv)) for US only

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
3 February 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMMUNIZATION WITH PORPHYROMONAS GINGIVALIS PROTECTS AGAINST HEART DISEASE

(57) Abstract: The invention is directed to a method of preventing and treating a patient having a risk factor and/or a symptom of cardiovascular disease using an immunogenic composition comprising an immunogenically effective portion of Porphyromonas gingivalis in a pharmaceutically effective carrier substance, and a vaccine for same.

WO 2004/045550 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/37013

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/00, 39/02
US CL : 424/184.1, 234.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/184.1, 234.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
BIOSIS, SCISEARCH, VETU, VETB, AGRICOLA, JAPIO, USPATFUL, EUROPATFUL

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MEDLINE, PUBMED

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database EMBASE on STN, AN:1999208848, DESHPANDE, R.G. ET AL, Invasion strategies of the Oral Pathogen Porphyromonas gingivalis: Implication for Carovascular Disease, Invasion and Metastasis, 1998, Vol.18, No. 2, pages 57-69. See the Abstract.	1-7
Y	Database MEDLINE on STN, AN:1998389923, HERZBERG, M C. ET AL, Dental Plaque, Platelets and Carovascular Diseases, Annals of Periodontology, The American Academy of Periodontology, July 1988, Vol. 3, No. 1, pages 151-160. See the Abstract.	1-7
Y	Database EMBASE on STN, AN:1998417201, LAMONT, R.J. ET AL, Life Below the Gum Line: Pathogenic Mechanisms of Porphyromonas gingivalis, Microbiology and Molecular Biology Reviews, 1998, Vol. 62, No. 4, pages 1244-1263. See the Abstract.	1-7
Y	Database EMBASE on STN, AN:2001371735, LOESCHE, W.J. ET AL, Peridontal Disease as a Specific, Albeit Chronic, Infection: Diagnosis and Treatment, Clinical Microbiology Reviews, 2001, Vol. 14, No. 4, pages 727-752. See the Abstract.	1-7



Further documents are listed in the continuation of Box C.



See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"B" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

30 March 2004 (30.03.2004)

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Date of mailing of the international search report

08 DEC 2004

Authorized officer

Vanessa L. Ford

Telephone No. 571.272.1600

INTERNATIONAL SEARCH REPORT

PCT/US03/31013

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database BIOSIS on STN, AN:2002:176618, CHEN, Z. ET AL., Protease-active Extracellular Protein Preparations for Porphyromonas gingivalis, Abstracts of the General Meeting of the American Society for Microbiology, 2001, Vol. 101, pages. 117-118. See the Abstract.	1-7
Y	Database CABI on STN, AN:2000:145383, WHITAKER ET AL., Effect of an Essential Oil-containing Antiseptic Mouthrinse on Induction of Platelet Aggregation by Oral Bacteria In Vitro, Journal of Clinical Periodontology, 2000, Vol. 27, No.5, pages 370-373. See the Abstract.	1-7
X	SHAPIRA ET AL., The Effects of Stress on the Inflammatory Response to Porphyromonas gingivalis in a Mouse Subcutaneous Chamber Model, Journal of Periodontology, March 1999, Vol. 70, No. 3, pages 289-292. See the entire document.	8-12
X	VASEL ET AL., Shared Antigen of Porphyromonas gingivalis and Bacteroides forsythus, Oral Microbiology and Immunology, 1996, Vol. 11, No. 4, pages 226-235. See the entire document.	8-12
X	GENCO ET AL., A Peptide Domain on Gingipain R Which Confers Immunity Against Porphyromonas gingivalis Infection in Mice, Infection and Immunity, September 1998, Vol. 66, No. 9, pages 4108-4114. See the entire document.	8-12
X	GENCO ET AL., Influence of Immunization of Porphyromonas gingivalis Colonization and Invasion in the Mouse Chamber Model, Infection and Immunity, April 1992, Vol. 60, No. 4, pages 1447-1454. See the entire document.	8-12
X	HOUSTON ET AL., Response of Guinea Pigs to a Vaccine Containing a New Adjuvant (SAF) and Gram-Negative Bacteria, Laboratory Animal Science, February 1995, Vol. 45, No. 1, p. 58-66. See the entire document.	8-12
X	EVANS ET AL., Immunization with Porphyromonas (Bacteroides) gingivalis Fimbriae Protects Against Periodontal Destruction, Infection and Immunity, July 1992, Vol. 60, No. 7, pages 2926-2935. See the entire document.	8-12
X	PERSSON ET AL., Immunization Against Porphyromonas gingivalis Inhibits Progression of Experimental Periodontitis in Nonhuman Primates, Infection and Immunity, March 1994, Vol. 62, No. 3, pages 1026-1031. See the entire document.	8-12
X	FROLOV ET AL., In vivo Exposure to Porphyromonas gingivalis up-regulates Nitric Oxide but Suppresses Tumour Necrosis Factor-Production by Cultured Macrophages, Immunology, March 1998, Vol. 93, No. 3, pages 323-328. See the entire document.	8-12
X	ZUBERY ET AL., Bone Resorption Caused by Three Periodontal Pathogens In Vivo in Mice Is Mediated in Part by Prostaglandin, Infection and Immunity, September 1998, Vol. 66, No. 9, pages 4158-4162. See the entire document.	8-12